

HPV FORM

Summary of Responses to the OECD Request for
Available Data on HVP Chemicals

0. General InformationName of Sponsor country **United States of America**

Contact point (name, address, telephone and telefax)

Name of Lead organisation

1. Chemical Identity* 1.1 CAS_number **123-38-6**

* 1.2 Name (give the name supplied by the OECD)

Propionaldehyde

1.3 Common Synonyms

Propanal
Propylaldehyde
Propyl Aldehyde
Methylacetaldehyde
Propionic Aldehyde
Propylic Aldehyde
UN 1275
OHS19740

1.4 Empirical formula **C₃H₆O**

* 1.5 Structural formula **CH₃-CH₂-CH^O**

1.6 Purity of industrial product

1.6.1 Degree of purity (percentage by weight/volume)

1.6.2 Identify of major impurities

1.6.3 Essential additives (stabilizing agents, inhibitors,
other additives), if applicable

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Physical-Chemical Data

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2.1 Melting or Decomposition Point

- 80° Centigrade

Method (e.g. OECD, other):

GLP: YES []

NO [X]

Comments: **Freezing point**

Reference: **Union Carbide Chemicals and Plastics Co.
Solvents & Coatings Materials Division
Material Safety Data Sheet**

2.2 Boiling Point

(including temperature of decomposition, if relevant).

48°C at 760 mm Hg kPa

Method (e.g., OECD, other):

GLP: Yes []

No [X]

Comments:

Reference: **Union Carbide Chemicals and Plastics Co.
Solvents & Coatings Materials Division
Material Safety Data Sheet**

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2.3 Vapour pressure

258 mm Hg at 20°C**kPa at 25°C (calculated)**

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Method (e.g. OECD, other):

GLP YES []

NO [X]

Comments:

Reference: **Union Carbide Chemicals and Plastics Co.
Solvents & Coatings Materials Division
Material Safety Data Sheet**

2.4 Partition coefficient n-Octanol/water

log P_{ow} = 0.83 at 23°C

Method: calculated [X]

- measured []

GLP: YES []

NO [X]

Analytical Method:

Comments (e.g., is the compound surface active or dissociative?):

Reference: **Verschuern, K. (1983) *Handbook of Environmental Data on Organic Chemicals*, 2nd Ed., Van Nostrand Reinhold, NY.**

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2.5 Water solubility **22% at 20°C**

Method (e.g., OECD, others):

GLP: YES []

NO [X]

Analytical Method:

Comments (e.g., the detection limit for insoluble substances):

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Reference: **Union Carbide Chemicals and Plastics Co.
Solvents & Coatings Materials Division
Material Safety Data Sheet**

2.6 Flash point (liquids)

<-18°C closed cup [X]; <-18°C open cup [X]

Method (e.g., OECD, other including reference to the standard used): **Tag**

GLP: YES []
NO [X]

Comments:

Reference: **Union Carbide Chemicals and Plastics Co.
Solvents & Coatings Materials Division
Material Safety Data Sheet**

2.7 Flammability (solid/gases)

Method (e.g., OECD, others):

GLP: YES []
NO [X]

Test results:

Lower Flammable Limit Air **2.6%**
Upper Flammable Limit Air **17.0%**

Comments:

Reference: **Union Carbide Chemicals and Plastics Co.
Solvents & Coatings Materials Division
Material Safety Data Sheet**

2.8 pH in water

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pH 7.5 at 85 mg/l (water)
pK_a

Method (e.g., OECD, other):

GLP: YES []
 NO [X]

Comments: **Initial pH in Fathead Minnow acute toxicity study**
 References: **Waggy, G. T. and J. R. Payne (1974) "Environmental Impact Analysis - Acute Aquatic Toxicity Testing". Project Report 910F44, Union Carbide Corporation, South Charleston Technical Center, South Charleston, WV.**

2.9 Other data e.g., relative density, surface tension (of aqueous solution), fat solubility, explosivity, oxidising properties and particle size distribution

Comments: **Henrys Law Constant H=3.32 atms/mole fraction (Calculated)**

References: **Fed. Reg. 59:78 April 2nd, February, 1994., p19610**

3. Source of Exposure

- * 3.1 Production levels expressed as tonnes per annum **150 to 175. The estimated annual production of propionaldehyde in the United States is in the order of 275 million pounds. Worldwide, it is estimated that 405 million pounds of this aldehyde are produced annually.**

Information on production levels should be provided in ranges (e.g., 100-1000 tonnes, ect.) per responder or country and the date for which those ranges apply should be given.

3.2 Processes **See attached Figure 1**

Describe sources of potential human or environmental exposure including workplace concentrations and emission data (in % release), if available, for both manufacturing and user areas.

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Typically, propionaldehyde is manufactured by the catalytic hydroformylation of ethylene with carbon monoxide and hydrogen (Oxo Process). The reaction is carried out under high pressure in closed systems. Crude propionaldehyde is stripped of dissolved gasses and heavy residuals by gas stripping in pressured columns and stored for downstream derivatives production. Characteristically, propionaldehyde production units are designed to vent possible emissions from reactors, columns and storage tanks to the plant fuel system. In addition other steps are taken to reduce emissions. Union Carbide, for instance, operates their "Oxo" unit under the "New Source Performance Standards (NSPS)" rule which requires fugitive emissions monitoring of all size valves on a quarterly basis and all pumps and compressors on a monthly basis. In Figure 1 a block diagram of a typical manufacturing unit is shown.

Propionaldehyde is stored in pressured tanks or tanks equipped with internal floating roofs in order to minimize losses by evaporation. Field storage tanks are either pressure storage tanks or blanketed with nitrogen over floating roofs. Propionaldehyde inventories are purposely maintained at the lowest workable level to insure quality is maintained. Processes which use propionaldehyde as a reactive intermediate are conducted in closed manufacturing systems designed to prevent exposure of personnel to the aldehyde and other potential monomers. Figure 2 is a block diagram illustrating a typical manufacturing and distribution plan.

Distribution:

For internal plant uses, propionaldehyde typically is transported by pipeline. We are not aware of any manufacturing process in which this volatile aldehyde would be handled in open containers. Tank cars (rail cars) and tank trucks are used for shipment to domestic customers. In loading these transport vehicles, vapor is collected from the closed tank, routed to a vent collection system and incinerated.

Fugitive Emissions:

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In the United States, for the year 1990, there were 18 facilities which reported environmental release information under provisions of the Super Fund Amendment Reauthorization Act (SARA). These were facilities either which manufactured or processed 25,000 pounds or more, or used more than 10,000 pounds of propionaldehyde. The toxic release inventory indicates that these facilities collectively released 988,986 pounds of propionaldehyde into the air and 34,885 pounds to other segments of the environment. In 1992, TRI reports were received from 22 submitters which collectively released 689,640 pounds to the air and 63949 pounds to other segments of the environment representing a total decrease of $\approx 25\%$

Workplace Monitoring:

In typical propionaldehyde operations, monitoring is conducted to assure that worker exposure is maintained well within acceptable exposure limits. No formal exposure standards have been established for this aldehyde, however, personnel monitoring within the Union Carbide production facility indicate that the 8-hour time weighted average (TWA) exposures are low. In the 17 year period between 1975 and 1992, a total of 73 personnel samples have been taken within the "Oxo" production unit. Of these, 62 ($\approx 85\%$) were below the detection limit of 0.01 ppm. The maximum TWA measured over this interval was 26 ppm and the geometric mean for all 73 TWA determinations was ≈ 0.2 ppm. In the same time frame 16 TWA determinations were made within the In-Plant Distribution Department. Of these 8 (50%) were below the detection limit of 0.01 ppm. In one or two instances excursions in the range of 100 ppm were determined, but the geometric mean for all 16 samples was still in the range of 1 ppm. We believe that these low personnel exposures are typical of the industry as a whole. Considering the low concentrations of propionaldehyde measured within the production unit, air concentrations at the fence-line and within the surrounding community must be extremely low.

In addition, area monitors are used in manufacturing areas to detect leaks and alert operating personnel to any unusual conditions which might result in episodic release of the aldehyde to the environment. Personnel protective equipment is maintained and available for immediate use in the event of unforeseen emergency situations.

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Reference:

- * 3.3 Information concerning Uses (including categories and types of uses expressed in percentage terms)

Examples of use categories are dyestuffs, intermediates, solvents, adhesives, building material agents, detergents, cleaning agents, fertilisers, plastic agents, surface treatment agents, etc.

Types of uses are divided into three: industrial use (open system and closed system), public use and export

Of the total production volume, it is believed that greater than 99% is used as an internal plant chemical intermediate. The major uses of propionaldehyde is as a reactive intermediate in the manufacture of n-propanol, propionic acid, 2-methyl pentanol, trimethylethane polyols, polyethylene additives, fragrance chemicals and fungicides. Propionaldehyde, being a reactive chemical intermediate, is not directly used in products reaching the consumer. Because of its reactive nature and volatility, residual concentration of propionaldehyde in consumer products is very low.

- 3.4 Options for disposal

Mode of disposal (e.g., incineration, release to sewage system) for each category and type of use, if appropriate; recycling possibility

-- Incineration in the event of a spill --

- 3.5 Other remarks

Reference: **-- None --**

4.0 Environmental Fate and Pathways

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Reporting of studies should give the test method, test conditions (lab versus field studies), test results (e.g., % degradation in specified time period) and reference. Information on breakdown products (treatment and stable) should be provided when available.

4.1 Degradability (biotic and abiotic) **Photooxidation**

Test substance: **Propionaldehyde**

In the case of poorly soluble chemicals, treatment given
(nature, concentration, ect.):

Test method (e.g., OECD, ISO, others):

GLP YES ☐
NO ☒

Test results: **T1/2 in air = 5.8 hours**

Comments: **Calculated**

Reference: **Software "Atmospheric Oxidation Program" (AOP) v. 1.43 developed by the Syracuse Research Corporation, an adaptation of the "Atkinson estimation methodology" for estimating hydroxyl radical and ozone reaction rates with organic compounds in air and based on the following two published references**
1. *Int. J. Chem. Kinet.* 19:799-828 (1987).
2. *Env. Toxic Chem.* 7:435-42 (1988).

4.1.1 Biodegradability

Test substance: **Propionaldehyde**

Test type, aerobic ☐, anaerobic ☒

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Test medium: water, water-sediment, soil, sewage treatment

Unacclimated domestic treatment plant water

In the case of poorly soluble chemicals, treatment given (nature, concentration, ect.):

Test method (e.g., OECD, ISO, others):

GLP YES ☐
NO ☒

Test results: **BOD/COD(theoretical)X100 = 70% (5-days); 83% (10-days); 80% (15-days); 95% (20-days)**

Comments:

Reference: **Waggy, G. T. and J. R. Payne (1974) "Environmental Impact Analysis - Product Biodegradability Testing". Project Report 910F44, Union Carbide Corporation, South Charleston Technical Center, South Charleston, WV.**

4.1.2 Sewage Treatment

Information on treatability of the substance -- **No data submitted** 4.1.3
Stability in air (e.g., photodegradability) and in water (e.g., hydrolysis)

Test substance: **Propionaldehyde**

Test method or estimation method (e.g., OECD, others):

-- No data submitted --

4.1.4 Identification of main mode of degradability in actual use

-- No data submitted --

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4.2 Bioaccumulation

Test substance: **Propionaldehyde**Test method (e.g., OECD, other): **-- No data submitted --**

4.3 Transport and distribution between environmental compartments including estimate environmental concentrations and distribution pathways

-- No data submitted --4.4 Monitoring data (environment) **-- No data submitted --**5. Ecotoxicological Data

5.1 Toxicity to fish

5.1.1 Results of acute tests

Test substance: **Propionaldehyde**Test species: **1) *Poecilia reticulata* (Guppy)**
2) *Pimephales promelas* (Fathead Minnow)

Test method (e.g., OECD, others):

- 1) o Type of test: static [], semi-static [**X**], flow-through []
- 2) o Type of test: static [**X**], semi-static [], flow-through []
- o Other (e.g., field test) []

GLP YES []
NO [**X**]

Test results:

LC50 or EC50 - values after 24, 48, 72 and 96 hours and method used to calculate these values

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- 1) LC50 = 15 mg/l (14-Day) [log LC50 2.41 when LC50 in units of umoles/liter]
- 2) LC50 = 85 mg/l (24-hours); 16 mg/l (48-hours); 14 mg/l (96-hours).

Comments:

Reference:

- 1) Deneer, J. W., Seinen, W. and J. L. M. Hermens (1988) "The Acute Toxicity of Aldehydes to the Guppy". *Aqu. Tox.* 12:185-192.
- 2) Waggy, G. T. and J. R. Payne (1974) "Environmental Impact Analysis - Acute Aquatic Toxicity Testing". Project Report 910F44, Union Carbide Corporation, South Charleston Technical Center, South Charleston, WV.

5.1.2 Results of long-term tests e.g., prolonged toxicity, early life-stage

-- No data submitted --

Test substance: **Propionaldehyde**

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5.2 Toxicity to daphnids

5.2.1 Results of acute tests

Test substance: **Propionaldehyde**

Test species: *Daphnia magna*

Test method (e.g., OECD, others):

GLP YES [X]

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NO []

Test results:

EC50 - values after 24 and 48 hours, and method used to calculate these values

24-Hour EC50 = 200 mg/l (95% Confidence interval 176 to 234 mg/l)**48-Hour EC50 = 125 mg/l (95% Confidence interval 106 to 147 mg/l)**

Comments:

Reference:

Union Carbide Corporation, Union Carbide Technical Center, South Charleston , WV. Acute Toxicity of Propionaldehyde to *Daphnia magna*. Environmental Products Testing Study No. 920420002. Draft dated June, 1992.

5.2.2 Results of long-term tests e.g., reproduction

-- No Data Submitted --Test substance: **Propionaldehyde**

*5.3

Toxicity to algae

Test substance: **Propionaldehyde**Test species: *Selenastrum capricornutum*

Test method (e.g., OECD, others):

4-day old algal culture maintained in controlled temperature environmental chamber at pH 7.5 under static conditions. The cultures were maintained for 96 hours at propionaldehyde concentrations of 3.13, 6.25, 12.5, 25, 50, 100, 200 and 400 mg/L.

GLP YES [X]

NO []

Test results:

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EC50 (duration, e.g. 24, 48, 72 hours)

24-Hour EC50 = 290 mg/L (95% confidence interval 210 to 480)

48-Hour EC50 = 133 mg/L

72-Hour EC50 = 58 mg/L (95% confidence interval 29 to 134)

96-Hour EC50 = 40 mg/L (95% confidence interval 20 to 80)

Maximum concentration at which no effect was observed within the period of the test. **25 mg/L - 96-hour**

Minimum concentration at which no effect was observed within the period of the test.

Comments:

Reference:

Union Carbide Corporation, Union Carbide Technical Center, South Charleston , WV. Acute Toxicity of Propionaldehyde to *Selenastrum capricornutum* Environmental Products Testing Study No. 920420001. Draft dated June, 1992.

5.4 Toxicity to other aquatic organisms

Test substance: **Propionaldehyde**

Test species: *Aedes aegypti* larvae (mosquito)

Test method (e.g., OECD, others):

- o Type of test: static [**X**], semi-static [], flow-through []
- o Other (e.g., field test) []

GLP YES []

NO [**X**]

Test results:

LC50 or EC50 values (acute) **LC50 = 0.25% (w/v)**

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Maximum concentration at which no effect was observed within the period of the test (prolonged test).

Minimum concentration at which no effect was observed within the period of the test (prolonged test)

Comments: **No details given as to concentrations used.**

Reference: **Kramer, V. C., Schnell, D. J. and K. W. Nickerson (1983)
"Relative Toxicity of Organic Solvents to *Aedes aegypti*
Larvae". *J. Invert. Path.* 42:285-287.**

5.5 Toxicity to bacteria

Test substance: **Propionaldehyde**

Test species: Sewage Microorganisms

Single species tests such as "Microtox Photobacterium luminescence test" and tests on overall processes such as nitrification or soil respiration are included in this item.

Test method (e.g., OECD, others):

oType of test Median inhibition concentration (IC₅₀) when resulting turbidity is at 50% of the control after a 6-hour incubation at 23°C [☐].

oOther (e.g., field observation) [☐]

GLP YES [☐]
NO [☒]

Test results: **IC₅₀ = 207 mg/l**

Comments:

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Reference: **Waggy, G. T. and R. L. Blessing (1987) "Environmental Impact Analysis - Acute Aquatic Toxicity Testing".**
File NO: 35269, Union Carbide Corporation,
South Charleston Technical Center, South Charleston, WV.

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5.6 Toxicity to terrestrial organisms

5.6.1 Toxicity to soil dwelling organisms -- **No data submitted --**

Test substance: **Propionaldehyde**

5.6.2 Toxicity to plants

Test substance: **Propionaldehyde**

Test species: ***Lactuca sativa* (Great Lakes Lettuce)**

Test method (e.g., OECD, others): **Seed Germination**

GLP YES ☐
 NO ☒

Test results:

EC50 for 7 and 14 days or LC50

13.7 mM propionaldehyde solution produced 50% inhibition of germination.

Maximum concentration at which no effect was observed within the period of the test.

Minimum concentration at which no effect was observed within the period of the test.

Comments:

Reference: **Reynolds, T. (1977) "Comparative Effects of Aliphatic Compounds on Inhibition of Lettuce Fruit Germination".**
***Ann. Bot.* 41:637-648.**

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5.6.3 Toxicity to birds -- **No data submitted** --Test substance: **Propionaldehyde**

5.7 Biological Effects Monitoring (including biomagnification)

-- **No data submitted** --

Studies on variation of predominant species in certain ecosystems and monitoring of biological effects (e.g., thinning of eggshell) etc. are included.

Test substance: **Propionaldehyde**

5.8 Biotransformation and kinetics in environmental species

-- **No data submitted** --

Under this item, studies on absorption, distribution, metabolism and excretion etc. should be given.

6.0 Toxicological Data (oral, dermal and inhalation, as appropriate)

Where observation on humans are available, e.g., irritation, these should be entered in the appropriate "Comments" section.

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6.1 Acute toxicity

6.1.1 Acute oral toxicity

Test substance: **Propionaldehyde**

Test species/strain:

- 1) **Male albino rats**
- 2) **Rat**
- 3) **Male & Female Sprague Dawley**

Test method (e.g., OECD, EC, limit test): **Gavage**

1) GLP YES [] 2) GLP YES [] 3) GLP YES [X]

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NO ☒ NO ☒ NO ☐
]

Test results:

LD50 or other measure of acute toxicity (e.g. in case of fixed dose test)

- 1) Oral LD50 - 1.41 g/Kg (95% confidence interval of 0.96 to 2.98)
- 2) Oral LD50 - 0.8 to 1.6 g/Kg
- 3) Oral LD50 - Males 2g/Kg killed 2 of 3;
 Females LD50 = 1.7 mg/Kg
 (95% Confidence interval 1.4 to 2.0 g/Kg)

Comments:

- 1) Administered as a 20% dispersion using a nonionic surfactant (1% TERGITOL "7") as a dispersion agent. Five animals used per dosage group.
- 3) Administered as an aqueous dilution at a dosage volume of 1ml/100g body weight. Rats observed for 14-days after dose administration. Study conducted under EPA TSCA Health Effects Test Guidelines.

Reference:

- 1) Union Carbide Corporation, Mellon Institute of Industrial Research Report 14-24 dated February 16, 1951.
- 2) Brabec, M. J. (1981) "Chapter 37: Aldehydes and Acetals in *Patty's Industrial Hygiene and Toxicology*, 3rd revised edition. Vol. 2A., Clayton, G. D. and F. E. Clayton, Eds. John Wiley & Sons, New York. p. 2643.
- 3) Union Carbide Corporation, Bushy Run Research Center Report 92U1030, Draft dated June 3, 1992.

6.1.2 Acute inhalation toxicity

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Test substance: **Propionaldehyde**

Test species/strain: 1) **Rats**
 2) **Male mature rats**
 3) **B6C3F1 & Swiss-Webster mice**
 4) **Fischer 344 rats**

Test method (e.g., OECD, EC, limit test):

GLP YES []

Test results:

LC50: 1) **26000 ppm (0.5 hours)**

Comments:

- 2) **Dynamically generated substantially saturated vapor killed 6 of 6 rats in 10 minutes, 2 of 6 rats in 5 minutes, and 0 of 5 in 2 minutes. Exposure to a measured concentration of 16000 ppm for 2.5-hours killed 6 of 6 rats, 8000 ppm killed 5 of 6 rats in 4-hours and 4000 ppm 0 of 6 rats in 4-hours.**
- 3) **The vapor concentration required to elicit a 50% decrease in respiratory rate (RD₅₀) of B6C3F1 mice was 2078 ppm (95% confidence interval 1803 to 2402), and in Swiss-Webster mice was 2052 ppm (95% confidence interval 1625 to 3040).**
- 4) **The vapor concentration required to elicit a 50% decrease in respiratory rate (RD₅₀) of Fischer 344 rats was 6789 ppm (95% confidence interval 3903 to 15466 ppm).**

Reference:

- 1) **Brabec, M. J. (1981) "Chapter 37: Aldehydes and Acetals**

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in *Patty's Industrial Hygiene and Toxicology*, 3rd revised edition. Vol. 2A., Clayton, G. D. and F. E. Clayton, Eds. John Wiley & Sons, New York. p. 2643.

- 2) Union Carbide Corporation, Mellon Institute of Industrial Research Report 15-55 dated June 30, 1952.**
- 3) Steinhagan, W. H. and C. S. Barrow (1984) *Toxicol. Appl. Pharmacol.* 72:495-503.**
- 4) Babiuk, C. Steinhagan, W. H. and C. S. Barrow (1985) *Toxicol. Appl. Pharmacol.* 79:143-149.**

6.1.3 Acute dermal toxicity

Test substance: **Propionaldehyde**

Test species/strain: 1) **New Zealand White Rabbits**
 2) **Guinea Pig**

Test method (e.g., OECD, limit test):

- 1) Application of undiluted test material for 24-hours to the skin under an occlusive dressing.**
- 2) No details given**
- 3) EPA TSCA Health Effects Test Guidelines**

1) GLP YES []	2) GLP YES []	3) GLP YES [X]
NO [X]	NO [X]	NO []

Test results:

LD50:

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- 1) **5.0 ml/Kg (95% confidence interval 3.4 to 7.5)**
- 2) **10 to 20 g/Kg**
- 3) **Males: 2.0 g/Kg killed 1 of 3.**
Females: LD50 = 2.5 g/Kg (95% Confidence interval 1.8 to 3.4 g/Kg)

Comments:

- 1) **Erythema and desquamation at the site of contact, pale and mottled livers and kidneys and congested lungs in victims.**
- 3) **24-Hour occluded application of undiluted test material to clipped skin with a 14-day observation period after application.**

Reference:

- 1) **Union Carbide Corporation, Mellon Institute of Industrial Research Report 15-55 dated June 30, 1952.**
- 2) **Brabec, M. J. (1981) "Chapter 37: Aldehydes and Acetals in *Patty's Industrial Hygiene and Toxicology*, 3rd revised edition. Vol. 2A., Clayton, G. D. and F. E. Clayton, Eds. John Wiley & Sons, New York. p. 2643.**
- 3) **Union Carbide Corporation, Bushy Run Research Center Report 92U1030, Draft dated June 3, 1992.**

6.2 Corrosiveness/Irritation

6.2.1 Skin Irritation

Test substance: **Propionaldehyde**

Test species/strain:

- 1) **New Zealand White Rabbits**
- 2) **Guinea Pig**
- 3) **New Zealand White Rabbits**

Test method (e.g., OECD, others):

- 1) **0.01 ml undiluted test substance applied to the uncovered clipped skin of the abdomen.**

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3) EPA TSCA Health Effects Test Guidelines. 4-Hour occluded application of 0.5 ml undiluted test material with 14-day observation period.

1) GLP YES [] NO [X] 2) GLP YES [] NO [X] 3) GLP YES [X] NO []

Test results: give maximum scores after hrs

- 1) **Marked erythema on 1 of 5 rabbits.**
- 2) **Severe irritation**
- 3) **Moderate to severe irritation with superficial necrosis. Irritation persisting on 4 of 6 rabbits at 14 days**

Comments:

- 1) **Instillation of .02 ml of undiluted test material into the inferior conjunctival sac of rabbit eyes produced severe injury, 0.005 ml instilled in an identical manner produced moderate damage.**
- 3) **Instillation of 0.1 ml into the inferior conjunctival sac of rabbit eyes produced mild transient corneal injury, iritis with moderate to severe conjunctival irritation and resolution of injury in all eyes by 10-days. 0.01 ml produced minor transient corneal injury, iritis and moderate to severe conjunctival injury with complete resolution in 7-days.**

Reference:

- 1) **Union Carbide Corporation, Mellon Institute of Industrial Research Report 15-55 dated June 30, 1952.**
- 2) **Brabec, M. J. (1981) "Chapter 37: Aldehydes and Acetals in Patty's Industrial Hygiene and Toxicology, 3rd revised edition. Vol. 2A., Clayton, G. D. and F. E. Clayton, Eds. John Wiley & Sons, New York. p. 2643.**

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**3) Union Carbide Corporation, Bushy Run Research Center Report
92U1030, Draft dated June 3, 1992.**

6.3 Skin sensitisation -- No data submitted --

Test substance: **Propionaldehyde**

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6.4 Repeated dose toxicity

Test substance: **Propionaldehyde**

Test species/strain: 1) **Alderley Park specific-pathogen-free rats**
2) **CD Male & Female Rats**

Test method (e.g., OECD, others):

- 1) **Propionaldehyde liquid injected at a known rate into a metered stream of air by means of a controlled, fluid-free atomizer.**
- 2) **OECD Screening Information Data Set Combined Repeated Dose/Reproductive Protocol**

1)	GLP	YES	[]	2)	GLP	YES	[X]
		NO	[X]			NO	[]

Test results:

- 1) **Four males and 4 females which received six, 6-hour exposures to 1300 ppm did not gain weight. Histological examination of tissues at necropsy revealed liver cell vacuolation. Four males and 4 females which received 20, 6-hour exposures to 90 ppm demonstrated no toxic signs and organs were normal at necropsy.**
- 2) **Male and female rats (15 per exposure group) were exposed to propionaldehyde by inhalation at air concentrations of 0, 150, 750 or 1500 ppm. Exposures were conducted 6-hours per day, 7-days per week. Males received 52 consecutive daily exposures, while females were exposed for 2-weeks prior to mating, during a 14-day (maximum) mating period and**

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through day 20 of gestation. No differences were observed between means of all three male exposure groups and controls with respect to body weight, body weight gain, clinical observations and food consumption. In females no exposure related clinical signs were noted, however, body weight gain and food consumption were significantly reduced in animals of this sex in the intermediate and high exposure groups during the first week of exposure and in the high exposure group during the first half of gestation. Food consumption was also slightly reduced in the females of the high and intermediate exposure groups either throughout, or during part of, gestation. Elevated erythrocyte count with accompanying increases in hemoglobin concentrations and hematocrit values and an increase in monocytes were noted in the males exposed to 1500 ppm. Kidney weights, as a percent of body weight were also slightly increased in males exposed to 1500 ppm. No exposure related increases in the incidence of gross lesions was apparent in either sex. The only exposure related finding upon microscopic examination of tissues was on the olfactory epithelium in the anterior 2 sections of the nasal cavities of both male and female rats. Vacuolization was primarily evident in the low and intermediate exposure groups with atrophy seen in the intermediate and high exposure groups. The injury appeared to be somewhat diminished in females possibly a result of a 6-day recovery period.

Dose or concentration at which no toxic effects were observed:

- 1) 90 ppm
- 2) No NOEL established for nasal lesions. 150 ppm for other manifestations of systemic toxicity

Comments:

Reference:

- 1) Gage, J. C. (1970) *Brit. J. Indust. Med.* 27:1-18.
- 2) Union Carbide Corporation, Bushy Run Research Center Report 91U0086 Draft dated June 17, 1992.

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6.5 Genetic toxicity

6.5.1 Bacterial test

Test substance: **Propionaldehyde**

Test species/strain:

- 1) *S. typhinurium* strains TA-100, TA-1535, TA-1537 & TA-98.
- 2) *S. typhinurium* strains TA-98, TA-100, TA-1535 & TA-1537
- 3) *S. typhinurium* strain TA-1535
- 4) *S. typhinurium* strain TA-98, TA-100 & TA-102

Test method (e.g., OECD, others):

Bacterial Forward Gene Mutation Assay in *Salmonella typhinurium*
(Ames Test)

GLP YES ☐
NO ☒

Test results:

Minimum concentration of test substance at which toxicity to bacteria was observed:

with metabolic activation:
without metabolic activation:

Concentration of test compound resulting in precipitation:

Genotoxic effects:

	+	?	-
1) with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
without metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

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		+	?	-
2)	with metabolic activation:	[]	[]	[X]
	without metabolic activation:	[]	[]	[X]
		+	?	-
3)	with metabolic activation:	[]	[]	[X]
	without metabolic activation:	[]	[]	[X]
		+	?	-
4)	with metabolic activation:	[]	[]	[X]

Comments:

- 1) **Five concentrations used ranging between 100 and 10000 ug/plate. Both rat liver S9 and Hamster liver S9 used for metabolic activation system**
- 3) **Six concentrations ranging between 0.01 and 2.5 umol/plate.**
- 4) **No plate counts given. Tested at concentrations between 0.13 nmoles and 0.13 mmoles per plate.**

Reference:

- 1) **Mortelmans, K., Haworth, S., Lawlor, T., Speck, W., Tainer, B. and E. Zeiger (1986) *Environ. Mut.* 8(suppl. 7): 1-119.**
- 2) **Florin, I., Rutberg, L., Curvall, M. and C. R. Enzell (1980) *Toxicol.* 18:219-232.**
- 3) **Pool, B. L. and M. Wiessler (1981) *Carcinogenesis* 2(10):991-997.**
- 4) **Aeschbacher, H. U., Wolleb, U., Loliger, J., Spadone, J. C. and R. Liardon (1989) "Contribution of Coffee Aroma Constituents to the Mutagenicity of Coffee". *Fd. Chem. Toxic.* 27:227-232.**

6.5.2 Non-bacterial *in vitro* test

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Test substance: **Propionaldehyde**

Type of cell used:

- 1) **CHO V79 HGPrt locus and Na⁺/K⁺ locus as resistance to Ouabain.**

Test method (e.g., OECD, others):

GLP YES ☐
NO ☒

Test results:

Lowest Concentration producing cell toxicity:

with metabolic activation:

without metabolic activation: **Approximately 30 mM**

Genotoxic effects:

	+	?	-
with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
without metabolic activation:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Comments:

- 1) **Propionaldehyde induced a dose dependent increase in the mutation frequency either at the HGPrt locus, with thioguanine as the selective agent, or at the Na⁺/K⁺ locus, with ouabain as the selective agent.**

Reference: **Brumbilla, G., Cajelli, E., Cunonero, R., Martelli, A. and A. M. Marinari (1989) "Mutagenicity in V79 Chinese Hamster Cells of n-Alkanals Produced by Lipid Peroxidation" *Mutagenesis* 4:277-279.**

6.5.3 Non-bacterial test *in vivo*

Test substance: **Propionaldehyde**

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Test species/strain: **Male & Female Swiss Webster Mice**

Test method (e.g., OECD, others):

Mouse Bone Marrow Micronucleus Test conducted in accordance with OECD Guidelines C(81)30(Final).

GLP YES ☒
NO ☐

Test results:

Lowest dose producing toxicity: The IP LD50 for combined sexes was determined as 960 mg/Kg body weight. Mice, 5 per sex per dose, received propionaldehyde by IP injection at either 0%, 25%, 50% or 80% of the LD50 (0, 240, 480 or 768 mg/Kg). No significant increases in the incidences of micronucleated PCEs were observed at 240 and 480 mg/Kg or in the 768 mg/Kg females. Increases in the incidence of micronucleated PCEs were observed in males receiving 768 mg/Kg at 24 and 48 hours, but not at 12 hours. There was no evidence that the increases in male mice were dose related and they were not considered biologically significant.

Effect on Mitotic Index or P/N Ratio:

PCE/NCE = 58% of Controls at 48-hours after injection in high dose females.

Genotoxic effects: + ? -
 [] [] [X]

Comments:

Reference: 2) **Union Carbide Corporation, Bushy Run Research Center Report 92U1011 Draft dated June 4, 1992.**

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6.6 Carcinogenicity -- No data submitted --

Test substance: **Propionaldehyde**

Test species/strain:

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6.7 Reproductive and Developmental toxicity

6.7.1 Reproductive toxicity

Test substance: **Propionaldehyde**Test species/strain: **CD Rats**

Test method (e.g., OECD, others):

**OECD Screening Information Data Set Combined Repeated
Dose/Reproductive Protocol**GLP YES ☒NO ☐

Test results:

Male and female rats (15 per exposure group) were exposed to propionaldehyde by inhalation at air concentrations of 0, 150, 750 or 1500 ppm. Exposures were conducted 6-hours per day, 7-days per week. Males received 52 consecutive daily exposures, while females were exposed for 2-weeks prior to mating, during a 14-day (Maximum) mating period and through day 20 of gestation. Females were allowed to litter and the offspring body weight, viability, disposition were monitored from birth until postnatal day 4. On day 4 of lactation, necropsies were performed on the adult females and the offspring were examined externally and sacrificed without pathologic evaluation. No significant effects of exposure were noted on any reproductive parameter assessed. Litter size and viability were similar among exposure groups and the control. Pup body weights on postnatal day 0 and 4 were not

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affected by exposure, although the body weight gain of pups from the high exposure group mothers for that period was slightly depressed.

NOEL for P generation: **No NOEL established for nasal lesions, 150 ppm for evidence of systemic toxicity.**

NOEL for F1 generation

NOEL for F2 generation

Maternal and Paternal general toxicity: **Nasal lesions - 150 ppm.**

Signs of systemic toxicity - 750 ppm

Reproductive toxicity observed in parental animals (fertility, gestation, reproductive organotoxicity, etc.): **> 1500 ppm**

Reproductive toxicity observed in offspring (weights of litter, postnatal growth, viability, etc.): **>1500 ppm**

Comments:

Reference: **Union Carbide Corporation, Bushy Run Research Center Report 91U0086 Draft dated June 17, 1992.**

6.7.2 Teratogenicity/Developmental toxicity

Test substance: **Propionaldehyde**

Test species/strain: **Sprague-Dawley rats.**

Test method (e.g., OECD, others): **Intraamniotic injection on day 13 of gestation.**

GLP YES ☐

NO ☒

Test results:

NOEL for maternal animals

NOEL for offspring **100 ug/fetus**

Maternal general toxicity

Pregnancy and litter data

Foetal data (live/dead, sex, external defects, soft tissue and skeletal defects)

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Comments:

**Increased incidence of dead or resorbed fetuses at 1000 ug/fetus.
No increased incidence of maleformed fetuses up to the highest
concentration tested, 1000 ug/fetus.**

Reference: **Slott, V. L. and B. F. Hales (1985) *Teratology* 32:65-72.**

6.8 Specific toxicities (Neurotoxicity, immunotoxicity etc.)

6.9 Toxicodynamics, toxico-kinetics

1) The retention of propionaldehyde vapor in the respiratory tract dog was approximately 75 to 80% of the inhaled dose at air concentrations between 100 and 400 ppm (250 mg/m³ to 1000 mg/m³). Retentions of 75% to 80% were also measured in the dog at tidal volumes ranging from approximately 110 to 200 ml.

Egle, J. L. (1972) "Retention of Inhaled Formaldehyde, Propionaldehyde and Acrolein in the Dog". *Arch. Environ. Health* 25:119-124.

2) The activity of the liver cytosolic propionaldehyde dehydrogenase was 9.4 nmoles NADH/min/mg protein in control mice and 19 nmoles NADH/min/mg protein in pregnant mice at an initial propionaldehyde concentration of 5 mM. Mitochondrial activity was 34.1 and 33.0 nmoles NADH/min/mg protein at a concentration of 5 mM, and 12.95 and 12.45 nmoles NADH/min/mg protein at a concentration of 50 uMin in control and pregnant mice respectively. The apparent K_m value for the enzyme using propionaldehyde as a substrate was approximately 0.36 mM in control mice and 0.37 mM in pregnant mice. Values using acetaldehyde were 0.59 and 0.56 mM, respectively.

Reference:

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Petersen, D. R., Panter, S. S. and A. C. Collins (1977) "Ethanol and Acetaldehyde Metabolism in the Pregnant Mouse". *Drug Alc. Depend.* 2:409-420.

7. Experience with Human Exposure (give full description of study design, effects of Accidental or Occupational Exposure, epidemiology)

Odor threshold of aqueous solutions for normal individuals, 145 ppb, for anosmic individuals, 656 ppb.

Amoore, J. E., Forrester,, L. J. and P. Pelosi (1976) "Specific Anosmia to Isobutyraldehyde: The Malty Primary Odor". *Chem. Senses Flavor* 2:17-25.

- 7.1 Biological Monitoring (including clinical studies, case reports, etc.)

No Data Available

8. Recommended Precautions, Classification (use and/or transporation) and Safety Data Sheets.

See attached Material Safety Data Sheets

9. Availability and references(s) for existing review(s)

Available

- 10 Name of responder

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Appendix I

Flow Diagram of Propionaldehyde Production Facility

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Appendix II

Union Carbide Material Safety Data Sheet for Propionaldehyde

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